

Cell 4.8 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

Applicants : Raju Kucherlapati et al.
Application No. : 10/656,623 Confirmation No.: Not yet assigned
Filed : September 4, 2003
For : HUMAN ANTIBODIES DERIVED FROM IMMUNIZED XENOMICE
Group Art Unit : Not yet assigned
Examiner : Not yet assigned

New York, New York
January 16, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

**TRANSMITTAL LETTER FOR
INFORMATION DISCLOSURE STATEMENT**

Sir:

Transmitted herewith is an Information Disclosure Statement in the above-identified application. This Statement is submitted:

- within three months of the application filing date;
- more than three months from the application filing date but before the mailing date of the first Office Action on the merits.

In accordance with 37 C.F.R. § 1.97, submission of this Statement requires no fee. However, if for any reason a fee is due, the Director is hereby authorized to

charge payment of any fees required in connection with this Information Disclosure Statement to Deposit Account No. 06-1075.

Respectfully submitted,



Jane T. Gunnison (Reg. No. 38,479)

Attorney for Applicants

R. Minako Pazdera (Reg. No. 46,984)

Agent for Applicants

c/o FISH & NEAVE

Customer No. 1473

1251 Avenue of the Americas

New York, New York 10020-1104

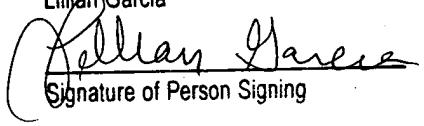
Tel.: (212) 596-9000

Fax.: (212) 596-9090

I hereby certify that this
Correspondence is being
deposited with the U.S.
Postal Service as First
Class Mail in an envelope
Addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450 on

January 16, 2004

Lillian Garcia


Signature of Person Signing



Cell 4.8 CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENT APPLICATION

Applicant(s) : Raju Kucherlapati et al.
Application No. : 10/656,623 Confirmation No.: Not Yet Assigned
Filed : September 4, 2003
For : HUMAN ANTIBODIES DERIVED FROM IMMUNIZED XENOMICE
Group Art Unit : Not Yet Assigned
Examiner : Not Yet Assigned

New York, New York 10020
January 16, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants make of record the following documents:

U.S. Patents

<u>Applicant</u>	<u>Patent No.</u>	<u>Issue Date</u>
Boss et al.	4,816,397	March 28, 1989
Bertling	4,950,599	August 21, 1990
Taketo	4,959,313	September 25, 1990

Fell et al.	5,204,244	April 20, 1993
Lonberg et al.	5,545,806	August 13, 1996
Surani et al	5,545,807	August 13, 1996
Donehower et al.	5,569,824	October 29, 1996
Lonberg et al.	5,569,825	October 29, 1996
Krimpenfort et al.	5,591,669	January 7, 1997
Kucherlapati, et al.	6,150,584	November 21, 2000

Foreign Publications

<u>Publication No.</u>	<u>Publication Date</u>
AU-B-15172/95	July 10, 1995
EP 0 298 807 A1	June 17, 1988
EP 0 315 062	May 10, 1989
EP 0 322 240	June 28, 1989
EP 0 459 372 A3	May 28, 1991
EP 0 463 151	January 2, 1992
WO 90/04036	April 19, 1990
WO 91/00906	January 24, 1991
WO 91/10741	July 25, 1991
WO 92/03918	March 19, 1992
WO 93/05165	March 18, 1993
WO 94/00569	January 6, 1994
WO 94/02602	February 3, 1994
WO 96/33735	October 31, 1996

Other Documents

Albertsen, et al., Construction and characterization of a yeast artificial chromosome library containing seven haploid human genome equivalents," *Proc. Natl. Acad. Sci.*, 87:4256-4260 (1990).

Aldhous, "Transgenic mice display a class (switching) act," *Science* 262:1212-1213 (1993).

Ayares, et al., "Sequence homology requirements for intermolecular recombination in mammalian cells," *Proc. Natl. Acad. Sci. U.S.A.*, 83:5199-5203 (1986).

Berman, et al., "Content and organization of the human Ig V_H locus: definition of three new V_H families and linkage to the Ig C_H locus," *EMBO J.*, 7:727-738 (1988).

Bird, et al., "Single-Chain Antigen-Binding Proteins," *Science*, 243:423-426 (1988).

Blankenstein, et al., "Immunoglobulin V_H region genes of the mouse are organized in overlapping clusters," *Eur. J. Immunol.*, 17:1351-1357 (1987).

Brinster, et al., "Introns increase transcriptional efficiency in transgenic mice," *Proc. Natl. Acad. Sci. USA*, 85:836-840 (1988).

Brownstein, et al., "Isolation of single-copy human genes from a library of yeast artificial chromosome clones," *Science*, 244:1348-1351 (1989).

Brüggemann, et al., "Human antibody production in transgenic mice: expression from 100kb of the human IgH locus," *European Journal of Immunology*, 21:1323-1326 (1991).

Brüggemann, et al., "Construction, function and immunogenicity of recombinant monoclonal antibodies," *Behring Inst. Mitt.*, 87:21-24 (1990).

Burke, et al., "Cloning of large segments of exogenous DNA into yeast by means of artificial chromosome vectors," *Science*, 236:806-812 (1987).

Buttin, G., "Exogenous Ig gene rearrangement in transgenic mice: a new strategy for human monoclonal antibody production?," *Trends in Genetics*, 3:205-206 (1987).

Capecci, et al., "Altering the Genome by Homologous Recombination," *Science*, 244:1288-1292 (1989).

Choi, et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome," *Nature Genetics* 4:117-123 (1993).

Choi, et al., "RNA splicing generates a variant light chain from an aberrantly rearranged κ gene," *Nature* 286:776-77- (1980).

Davies, et al., "Targeted alterations in yeast artificial chromosomes for inter-species gene transfer," *Nuc. Acids Res.*, 20:2693-2698 (1992).

Doelker, et al., "The CySF-L2 factor from dialysable human leucocyte extract activates natural killer cytotoxicity by induction of interferon γ," *Cancer Immunology Immunotherapy*, 34:299-305 (1992).

Doetschman, et al., "Targeted mutation of the HPRT gene in mouse embryonic stem cells," *Proc. Natl. Acad. Sci. USA*, 85:8583-8587 (1988).

Eisen, Herman N., "Immunology: An Introduction to Molecular and Cellular Principles of the Immune Responses," 349-351 (2d ed. 1989).

Eliceiri, et al., "Stable integration and expression in mouse cells of yeast artificial chromosomes harboring human genes," *Proc. Natl. Acad. Sci. USA*, 88:2179-2183 (1991).

Emery, et al., "Humanised monoclonal antibodies for therapeutic applications," *Expert Opinion on Investigational Drugs*, 3:241-251 (1994).

- Garza, et al., "Mapping the Drosophila genome with yeast artificial chromosomes with yeast artificial chromosomes," *Science*, 246:641-646 (1989).
- Gnirke, et al., "Cloning and *in vivo* expression of the human GART gene using yeast artificial chromosomes," *EMBO J*, 10(7):1629-1634 (1991).
- Green, L.L. et al., "Antigen-specific human monoclonal antibodies from mice engineered with human Ig heavy and light Chain YACs," *Nat. Genet.* 7:13-21 (1994).
- Griffiths, et al., "Isolation of high affinity human antibodies directly from large synthetic repertoires," *The EMBO Journal*, 13:3245-3260 (1994).
- Huxley, et al., "The Human HPRT gene on a yeast artificial chromosome is functional when transferred to mouse cells by cell fusion," *Genomics*, 9:742-750 (1991).
- Jakobovits, et al., "Germ-line transmission and expression of a human-derived yeast artificial chromosome," *Nature*, 362:255-258 (1993).
- James, et al., "Human Monoclonal Antibody Production: Current Status and Future Prospects," *Journal of Immunological Methods*, 100:5-40 (1987).
- Johnson, et al., "Targeting of Nonexpressed Genes in Embryonic Stem Cells Via Homologous Recombination," 245:1234-1236 (1989).
- Joyner, et al., "Production of a mutation in mouse En-2 gene by homologous recombination in embryonic stem cells," *Nature*, 338:153-155 (1989).
- Koller, et al., "Inactivating the β_2 -microglobulin locus in mouse embryonic stem cells by homologous recombination," *Proc. Natl. Acad. Sci.*, 86:8932-8935 (1989).
- Kucherlapati, R., "Homologous recombination in mammalian somatic cells," *Prog. Nucleic Acids Res. Mol. Biol.*, 36:301-310 (1989).
- Lenz, et al., "Expression of Heterobispecific Antibodies by Genes Transferred into Producer Hybridoma Cells," *Gene*, 87:213-218 (1990).
- Liu et al., "Chimeric mouse-human IgG1 antibody that can mediate lysis of cancer cells," *Proc Natl Acad Sci USA*, 84:3439-3443 (1987).
- Mansour, et al., "Disruption of the proto-oncogene *int-2* in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes," *Nature*, 336:348-352 (1988).
- Matsuda, et al., "Structure and physical map of 64 variable segments in the 3'0.8- megabase region of the human immunoglobulin heavy-chain locus," *Nature Genetics*, 3:88-94 (1993).
- Max, et al., "Sequences of five potential recombination sites encoded close to an immunoglobulin κ constant region gene," *Proc. Natl. Acad. Sci. USA*, 76:3450-3454 (1979).
- Miller, et al., "Structural alterations in J regions of mouse immunoglobulin lambda genes are associated with differential gene expression," *Nature*, 295:428-430 (1982).
- Morrison, S. "Success is Specification," *Nature*, 368:812-813 (1994).

- Mortensen, et al., "Production of homozygous mutant ES cells with a single targeting construct," *Mol. Cell. Biol.*, 12(5):2391-2395 (1992).
- Munker, et al., "Recombinant human TNF induces production of granulocyte-monocyte colony-stimulating factor," *Nature*, 323:79-82 (1986).
- Orkin, et al., "Mutation in an intervening sequence splice junction in man," *Proc. Natl. Acad. Sci. USA*, 78:5041-5045 (1981).
- Pachnis, et al., "Transfer of a yeast artificial chromosome carrying human DNA from *Saccharomyces cerevisiae* into mammalian cells," *Proc. Nat'l. Acad. Sci. USA*, 87:5109-5113 (1990).
- Pavan, et al., "Modification and transfer into an embryonal carcinoma cell line of a 360-kilobase human-derived yeast artificial chromosome," *Mol. Cell. Biol.*, 10(8):4163-4169 (1990).
- Queen, et al., "A humanized antibody that binds to the interleukin 2 receptor," *Proc. Natl. Acad. Sci. USA*, 86:10029-10033 (1989).
- Rajewsky, et al., "Evolutionary and somatic selection of the antibody repertoire in the mouse," *Science*, 238:1088-1094 (1987).
- Ramirez-Solis, et al., "Chromosome engineering in mice," *Nature*, 378:720-724 (1995).
- Sakano, et al., "Sequences at the somatic recombination sites of immunoglobulin light-chain genes," *Nature*, 280:288-294 (1979).
- Sakano, et al., "Two types of somatic recombination are necessary for the generation of complete immunoglobulin heavy-chain genes," *Nature*, 286:676-683 (1980).
- Sakano, et al., "Identification and nucleotide sequence of a diversity DNA segment (D) of immunoglobulin heavy-chain genes," *Nature*, 290:562-565 (1981).
- Schedl, et al., "Transgenic mice generated by pronuclear injection of a yeast artificial chromosome," 20:3073-3077 (1992).
- Schedl, et al., "A method for the generation of YAC transgenic mice by pronuclear microinjection," *Nucleic Acids Research*, 21:4783-4787 (1993).
- Schedl, et al., "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice," *Nature*, 362:258-261 (1993).
- Schwartzberg, et al., "Germ-line transmission of a c-abl mutation produced by targeted gene disruption in ES cells," 246:799-803 (1989).
- Seidman, et al., "A Mutant immunoglobulin light chain is formed by aberrant DNA- and RNA-splicing events," *Nature*, 286:779-783 (1980).
- Shimizu, et al., "Immunoglobulin double-isotype expression by trans-mRNA in a human immunoglobulin transgenic mouse," *Proc. Natl. Acad. Sci. USA*, 86:8020-8023 (1989).

Shin, et al., "Physical map of the 3' region of the human immunoglobulin heavy chain locus clustering of autoantibody-related variable segments in one haplotype," *EMBO J*, 10:3641-3645 (1991).

Strauss, et al., "Germ line transmission of a yeast artificial chromosome spanning the murine α_1 (I) collagen locus," *Science* 259:1904-1907 (1993).

Thomas, et al., "Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells," *Cell*, 51:503-512 (1987).

Traver, et al., "Rapid screening of a human genomic library in yeast artificial chromosomes for single-copy sequences," *Proc. Natl. Acad. Sci. USA*, 86:5898-5902 (1989).

Treisman, et al., "Specific transcription and RNA splicing defects in five cloned β -thalassaemia genes," 302:591-596 (1983).

Tucker, et al., "Mouse IgA heavy chain gene sequence: implications for evolution of immunoglobulin hinge exons," *Proc. Natl. Acad. Sci. USA*, 78:7684-7688 (1981).

Yancopoulos, et al., "Developmentally controlled and tissue-specific expression of unarranged V_H gene segments," *Cell*, 40:271-281 (1985).

Zachau, "The human immunoglobulin κ locus and some of its acrobatics," *Biol. Chem.*, 371:1-6 (1990).

Zijlstra, et al., "Germ-line transmission of a disrupted $\beta 2$ -microglobulin gene produced by homologous recombination in embryonic stem cells," 342:435-438 (1989).

Copies of all the documents listed above were submitted by applicants in parent U.S. Patent Application No. 08/923,138; or were cited by the Examiner during prosecution of the parent application. Pursuant to 37 C.F.R. §1.98(d), applicants have not enclosed copies of the listed documents herewith. However, applicants stand ready to provide copies at the Examiner's request.

Applicants request that the documents be: (1) fully considered by the Examiner during the course of examination of this application; and (2) printed on any patent that may issue

from this application. Applicants also request that a copy of the enclosed Form PTO-1449, duly initialed by the Examiner, be forwarded to the undersigned with the next official communication.

Respectfully submitted,

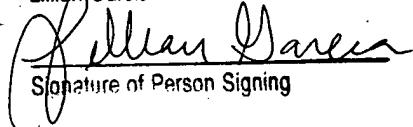


Jane T. Gunnison (Reg. No. 27,794)
Attorney for Applicants
R. Minako Pazdera (Reg. No. 46,984)
Agent for Applicants
c/o FISH & NEAVE
Customer No. 1473
1251 Avenue of the Americas
New York, New York 10020-1104
Tel.: (212) 596-9000
Fax.: (212) 596-9090

I hereby certify that this
Correspondence is being
deposited with the U.S.
Postal Service as First
Class Mail in an envelope
Addressed to:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450 on

January 16, 2004

Lillian Garcia



Lillian Garcia
Signature of Person Signing

FORM PTO-1449

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.
Cell 4.8 CONAPPLICATION NO.
10/656,623APPLICANT
Raju Kucherlapati et al.CONFIRMATION NO.
Not yet assignedFILING DATE
September 4, 2003GROUP
Not yet assignedINFORMATION DISCLOSURE
STATEMENT BY APPLICANT

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	4,816,397	03/28/89	Boss et al.	435	68	
	4,950,599	08/21/90	Bertling	435	172.3	
	4,959,313	09/25/90	Taketo	435	69.1	
	5,204,244	04/20/93	Fell et al.	435	69.6	
	5,545,806	08/13/96	Lonberg et al.	800	2	
	5,545,807	08/13/96	Surani et al	800	2	
	5,569,824	10/29/96	Donehower et al.	800	2	
	5,569,825	10/29/96	Lonberg et al.	800	2	
	5,591,669	01/07/97	Krimpenfort et al.	800	2	
	6,150,584	11/21/00	Kucherlapati, et al.	800	18	

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	AU-B-15172/95	07/10/95	Australia				
	EP 0 298 807 A1	17/06/88	Europe				
	EP 0 315 062	05/10/89	Europe				
	EP 0 322 240	06/28/89	Europe				
	EP 0 459 372 A3	28/05/91	Europe				
	EP 0 463 151	01/02/92	Europe				
	WO 90/04036	04/19/90	PCT				
	WO 91/00906	01/24/91	PCT				
	WO 91/10741	07/25/91	PCT				
	WO 92/03918	03/19/92	PCT				
	WO 93/05165	03/18/93	PCT				
	WO 94/00569	01/06/94	PCT				
	WO 94/02602	02/03/94	PCT				
	WO 96/33735	10/31/96	PCT				

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.8 CON	APPLICATION NO. 10/656,623
 INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT Raju Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 4, 2003	GROUP Not yet assigned

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Albertsen et al., "Construction and Characterization of a Yeast Artificial Chromosome Library Containing Seven Haploid Human Genome Equivalents," <i>Proc. Natl. Acad. Sci.</i> 87:4256-4260 (1990).
	Aldhous, "Transgenic mice display a class (switching) act," <i>Science</i> 262:1212-1213 (1993).
	Ayares, et al., "Sequence Homology Requirements for Intermolecular Recombination in Mammalian Cells," <i>Proc. Natl. Acad. Sci. USA</i> 83:5199-5203 (1986).
	Berman, et al., "Content and Organization of the Human Ig V _H Locus: Definition of Three New V _H Families and Linkage to the Ig C _H Locus," <i>EMBO J.</i> 7:727-738 (1988).
	Bird, et al., "Single-Chain Antigen-Binding Proteins," <i>Science</i> , 243:423-426 (1988).
	Blankenstein et al., "Immunoglobulin VH Region Genes of the Mouse Are Organized in Overlapping Clusters," <i>Eur. J. Immunol.</i> 17:1351-1357 (1987).
	Brinster, et al., "Introns Increase Transcriptional Efficiency in Transgenic Mice," <i>Proc. Natl. Acad. Sci., USA</i> , 85:836-840 (1988).
	Brownstein et al., "Isolation of Single-copy Human Genes from a Library of Yeast Artificial Chromosome Clones," <i>Science</i> 244:1348-1351 (1989).
	Brüggemann et al., "A Repertoire of Monoclonal Antibodies with Human Heavy Chains from Transgenic Mice," <i>Proc. Natl. Acad. Sci.</i> 86:6709-6713 (1989).
	Brüggemann et al., "Construction, Function and Immunogenicity of Recombinant Monoclonal Antibodies," <i>Behring Inst. Mitt.</i> 87:21-24 (1990).
	Brüggemann et al., "Human Antibody Production in Transgenic Mice: Expression from 100 Kb of the Human IgH Locus," <i>Eur. J. Immunol.</i> 21:1323-1326 (1991).
	Burke et al., "Cloning of Large Segments of Exogenous DNA into Yeast by Means of Artificial Chromosome Vectors," <i>Science</i> 236:806-812 (1987).
	Buttin, et al., "Exogenous Ig Gene Rearrangement in Transgenic Mice: A New Strategy for Human Monoclonal Antibody Production," <i>Trends in Genetics</i> 3(8):205-206 (1987).
	Capecci, et al., "Altering The Genome By Homologous Recombination," <i>Science</i> 244:1288-1292 (1989).
	Choi, et al., "RNA Splicing Generates a Variant Light Chain from an Aberrantly Rearranged κ Gene," <i>Nature</i> 286:776-779 (1980).
	Choi, et al., "Transgenic mice containing a human heavy chain immunoglobulin gene fragment cloned in a yeast artificial chromosome," <i>Nature Genetics</i> 4:117-123 (1993).
	Cox Declaration, from United States Patent No. 5,545,806.
	Davies et al., "Targeted Alterations in Yeast Artificial Chromosomes for Inter-species Gene Transfer," <i>Nucleic Acids Res.</i> 20:2693-2698 (1992).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.8 CON	APPLICATION NO. 10/656,623
O I P E S C T O INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT Raju Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 4, 2003	GROUP Not yet assigned

JAN 21 2004

PATENT & TRADEMARK OFFICE

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Doelker, et al., "The CySF-L2 factor from dialysable human leucocyte extract activates natural killer cytotoxicity by induction of interferon γ ," <i>Cancer Immunology Immunotherapy</i> , 34:299-305 (1992).
	Doetschman et al., "Targeted Mutation of the Hprt Gene in Mouse Embryonic Stem Cells," <i>Proc. Natl. Acad. Sci. USA</i> , 85: 8583-8587 (1988).
.	Dorfman, N.A., "The Optimal Technological Approach to the Development of Human Hybridomas," <i>J. Biol. Resp. Modif.</i> 4:213-239 (1985).
.	Eisen, Herman N., "Immunology: An Introduction to Molecular and Cellular Principles of the Immune Responses," 349-351 (2d ed. 1989).
	Eliceiri et al., "Stable Integration and Expression in Mouse Cells of Yeast Artificial Chromosomes Harboring Human Genes," <i>Proc. Natl. Acad. Sci.</i> 88:2179-2183 (1991).
	Emery, et al., "Humanised monoclonal antibodies for therapeutic applications," <i>Expert Opinion on Investigational Drugs</i> , 3:241-251 (1994).
	Garza et al., "Mapping the <i>Drosophila</i> Genome with Yeast Artificial Chromosomes," <i>Science</i> 246:641-646 (1989).
	Gnirke et al., "Cloning and in Vivo Expression of the Human GART Gene Using Yeast Artificial Chromosomes," <i>EMBO J.</i> 10(7):1629-1634 (1991).
	Green, et al., "Antigen-Specific Human Monoclonal Antibodies from Mice Engineered with Human Ig Heavy and Light Chain YACs," <i>Nature Genetics</i> 7:13-21 (1994).
	Griffiths, et al., "Isolation of high affinity human antibodies directly from large synthetic repertoires," <i>The EMBO Journal</i> , 13:3245-3260 (1994).
	Huxley et al., "The Human HPRT Gene on a Yeast Artificial Chromosome Is Functional When Transferred to Mouse Cells by Cell Fusion," <i>Genomics</i> 9:742-750 (1991).
	Jakobovits, et al., "Germ-Line Transmission and Expression of a Human-Derived Yeast Artificial Chromosome," <i>Nature</i> 362:255-258 (1993).
	James, et al., "Human monoclonal antibody production: current status and future prospects," <i>Journal of Immunological Methods</i> , 100:5-40 (1987).
.	Johnson, et al., "Targeting of Nonexpressed Genes in Embryonic Stem Cells Via Homologous Recombination," 245:1234-1236 (1989).
.	Joyner et al., "Production of a Mutation in Mouse En-2 Gene by Homologous Recombination in Embryonic Stem Cells," <i>Nature</i> 338:153-155 (1989).
	Koller et al., "Inactivating the β_2 -microglobulin Locus in Mouse Embryonic Stem Cells by Homologous Recombination," <i>Proc. Natl. Acad. Sci.</i> 86:8932-8935 (1989).
	Kucherlapati, R., "Homologous Recombination in Mammalian Somatic Cells," <i>Prog. Nucleic Acid Res. Mol. Biol.</i> 36:301-310 (1989).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.8 CON	APPLICATION NO. 10/656,623
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT Raju Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 4, 2003	GROUP Not yet assigned



OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

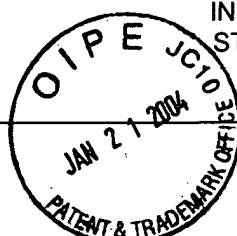
EXAMINER INITIAL	
	Lenz, et al., "Expression of heterobispecific antibodies by genes transferred into producer hybridoma cells," <i>Gene</i> , 87:213-218 (1990).
	Liu et al., "Chimeric mouse-human IgG1 antibody that can mediate lysis of cancer cells," <i>Proc Natl Acad Sci USA</i> , 84:3439-3443 (1987).
*	Mansour, et al., "Disruption of the Proto-Oncogene <i>Int-2</i> In Mouse Embryo-Derived Stem Cells: A General Strategy for Targeting Mutations to Non-Selectable Genes," <i>Nature</i> 336:348-352 (1988).
*	Matsuda et al., "Structure and Physical Map of 64 Variable Segments in the 3' 0.8-megabase Region of the Human Immunoglobulin Heavy-chain Locus," <i>Nature Genet.</i> 3:88-94 (1993).
	Max, et al., "Sequences of Five Potential Recombination Sites Encoded Close to an Immunoglobulin κ Constant Region Gene," <i>Proc. Natl. Acad. Sci., USA</i> 76(7):3450-3454 (1979).
	Miller, et al., "Structural Alterations in J Regions of Mouse Immunoglobulin λ Genes are Associated with Differential Gene Expression," <i>Nature</i> 295:428-430 (1982).
	Morrison, "Success in Specification," <i>Nature</i> , 368:812-813 (1994).
	Mortensen et al., "Production of Homozygous Mutant ES Cells with a Single Targeting Construct," <i>Mol. Cell. Biol.</i> 12(5):2391-2395 (1992).
	Munker, et al., "Recombinant human TNF induces production of granulocyte-monocyte colony-stimulating factor," <i>Nature</i> , 323:79-82 (1986).
	Orkin, et al., "Mutation in an Intervening Sequence Splice Junction in Man," <i>Proc. Natl. Acad. Sci. USA</i> 78(8):5041-5045 (1981).
	Pachnis et al., "Transfer of a Yeast Artificial Chromosome Carrying Human DNA from <i>Saccharomyces cerevisiae</i> into Mammalian Cells," <i>Proc. Natl. Acad. Sci.</i> 87:5109-5113 (1990).
	Pavan et al., "Modification and Transfer into an Embryonal Carcinoma Cell Line of a 360-kilobase Human-derived Yeast Artificial Chromosome," <i>Mol. Cell. Biol.</i> 10(8):4163-4169 (1990).
	Queen, et al., "A humanized antibody that binds to the interleukin 2 receptor," <i>Proc. Natl. Acad. Sci. USA</i> , 86:10029-10033 (1989).
	Rajewsky, et al., "Evolutionary and Somatic Selection of the Antibody Repertoire in the Mouse," <i>Science</i> 238:1088-1094 (1987).
	Ramirez-Solis, et al., "Chromosome Engineering in Mice," <i>Nature</i> 378:720-724 (1995).
*	Sakano, et al., "Sequences at the Somatic Recombination Sites of Immunoglobulin Light-Chain Genes," <i>Nature</i> 280:288-294 (1979).
	Sakano, et al., "Two Types of Somatic Recombination are Necessary for the Generation of Complete Immunoglobulin Heavy-Chain Genes," <i>Nature</i> 286:676-683 (1980).
	Sakano, et al., "Identification and nucleotide sequence of a diversity DNA segment (D) of immunoglobulin heavy-chain genes," <i>Nature</i> , 290:562-565 (1981).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. Cell 4.8 CON	APPLICATION NO. 10/656,623
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		APPLICANT Raju Kucherlapati et al.	CONFIRMATION NO. Not yet assigned
		FILING DATE September 4, 2003	GROUP Not yet assigned



OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	
	Schedl, et al., "Transgenic Mice Generated By Pronuclear Injection of a Yeast Artificial Chromosome," <i>Nucl. Acids Res.</i> 20:3073-3077 (1992).
	Schedl, et al., "A Method for the Generation of YAC Transgenic Mice by Pronuclear Microinjection," <i>Nucleic Acids Research</i> 21(20):4783-4787 (1993).
	Schedl, et al., "A yeast artificial chromosome covering the tyrosinase gene confers copy number-dependent expression in transgenic mice," <i>Nature</i> , 362:258-261 (1993).
	Schwartzberg et al., "Germ-Line Transmission of a c-abl Mutation Produced by Targeted Gene Disruption in ES Cells," <i>Science</i> 246:799-803 (1989).
	Seidman, et al., "A Mutant Immunoglobulin light Chain is Formed by Aberrant DNA- and RNA-Splicing Events," <i>Nature</i> 286:779-783 (1980).
	Shimizu, et al., "Immunoglobulin Double-Isotype Expression by Trans-mRNA in a Human Immunoglobulin Transgenic Mouse," <i>Proc. Natl. Acad. Sci., USA</i> 86:8020-8023 (1989).
	Shin et al., "Physical Map of the 3' Region of the Human Immunoglobulin Heavy Chain Locus: Clustering of Autoantibody-related Variable Segments in One Haplotype," <i>EMBO J.</i> 10:3641-3645 (1991).
	Strauss, W. M. et al., "Germ Line Transmission of a Yeast Artificial Chromosome Spanning the Murine $\alpha_1(I)$ Collagen Locus," <i>Science</i> 259:1904-1907 (1993).
	Thomas, et al., "Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells," <i>Cell</i> , 51:503-512 (1987).
	Traver, et al., "Rapid screening of a human genomic library in yeast artificial chromosomes for single-copy sequences," <i>Proc. Natl. Acad. Sci.</i> , 86:5898-5902 (1989)
	Treisman, et al., "Specific Transcription and RNA Splicing Defects in Five Cloned β -thalassaemia Genes," <i>Nature</i> 302:591-596 (1983).
	Tucker et al., "Mouse IgA Heavy Chain Gene Sequence: Implications for Evolution of Immunoglobulin Hinge Exons," <i>Proc. Natl. Acad. Sci.</i> 78:7684-7688 (1981).
	Yancopoulos, et al. "Developmentally Controlled and Tissue-Specific Expression of Unrearranged V_H Gene Segments," <i>Cell</i> 40:271-281 (1985).
	Zachau, "The Human Immunoglobulin κ Locus and Some of its Acrobatics," <i>Biol. Chem.</i> 371:1-6 (1990).
	Zijlstra, et al., "Germ-Line Transmission of a Disrupted β_2 -microglobulin Gene Produced by Homologous Recombination in Embryonic Stem Cells, <i>Nature</i> 342:435-438 (1989).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.